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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/913,435	02/02/2002	Edward J. Yurkow	RU-0130	9557
26259	7590	05/25/2006	EXAMINER	
LICATLA & TYRRELL P.C. 66 E. MAIN STREET MARLTON, NJ 08053			SPIVACK, PHYLLIS G	
			ART UNIT	PAPER NUMBER
			1614	

DATE MAILED: 05/25/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

09/913,435

Applicant(s)

Yurkow et al.

Examiner

Phyllis G. Spivack

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --
Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 24 March 2006.
- 2a) ☐ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1 and 5 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1, 5 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____ |

Applicants' Reply filed March 24, 2006 is acknowledged. Claims 1 and 5 remain under consideration.

A new title is noted.

Claim 1 is rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventors, at the time the application was filed, had possession of the claimed invention. The amendment to claim 1 filed August 23, 2005 lacks support in the specification. No reference to specification was provided by Applicants as to support for the recitation "non-viral" cells. See *In re Rasmussen*, 211 USPQ 323.

In the last Office Action claims 1 and 5 were rejected under 35 U.S.C. 102(b) as being anticipated by Qiu et al., The Journal of Biological Chemistry. It was asserted Qiu teaches a method of stabilizing or maintaining the redox state of hyperproliferative human colonic carcinoma cells, cell line HCT116, by contacting said cells with chemotherapeutic agents, aziridinybenzoquinones (AZQ), as required by claim 5, and a redox clamping agent, N-acetylcysteine (NAC). See page 31917, column two, under *Effects of N-acetylcysteine on Free Radical Production by HCT116 cells*. In this model involving abnormal cell growth or proliferation, redox cycling is described. The effect of N-acetylcysteine on free radical production by the quinones suggests an effective transfer of the radical character from an oxygen-centered radical to a less reactive sulfur-center radical in Reaction 2; i.e., the effect is dependent on its free thiol group.

With respect to claim 5, Applicants argue Qui fails to teach stabilizing abnormal fluctuations in the redox state associated with abnormal cell growth or proliferation because the abnormal redox state of the cells in the reference was associated with free radicals formed during the redox transitions of aziridinybenzoquinones. With respect to claim 1, Applicants argue the reference fails to teach sensitizing non-viral cells to the effects of a chemotherapeutic agent because the antioxidant blocks aziridinybenzoquinone-mediated induction of p21.

Applicants' arguments have been given careful consideration but are not found persuasive. The rejection of record is repeated for the reasons of record. Fluctuations in the redox state appear to regulate the transcription of genes that control proliferation. An interrelationship exists between the redox state and growth control. Treatment with NAC, a scavenger of reactive oxygen species, yields a more reducing redox state of some proliferating cells. It is the electron flow through side chain functional $\text{CH}_2\text{-SH}$ groups of cysteinyl residues that account for their redox-sensing properties.

Qui teaches stabilization of abnormal fluctuations in the redox state associated with abnormal growth during the metabolism of aziridinybenzoquinone by HCT 116 cells through the activity of N-acetylcysteine acting as an intracellular antioxidant. See page 31917, column 2, line 36. Intracellularly, NAC is rapidly hydrolyzed to release cysteine. In claim 5 "stabilizing" is broadly interpreted as holding steady, maintaining or limiting fluctuations; "abnormal" is broadly interpreted as "deviant or irregular; "specific" is broadly interpreted as particular or distinctive.

Qui teaches sensitizing, i.e., rendering responsive, receptive or susceptible, to the effects of AZQ, i.e., antitumor or cytotoxic effects, and the maintenance of HCT116 cells in a specific, i.e., particular, redox state comprising contacting said cells with AZQ and NAC. The strong superoxide anion component that is generated by AZQ is suppressed by NAC. The system, as disclosed by Qui, is dynamic with p21 a critical site of redox regulation. The exposure of HCT116 cells to NAC caused an increase in p21 (a cell cycle regulating gene) mRNA and thus contributed to the effects of AZQ as an antitumor agent. See Figures 3 and 7, A and B.

No claim is allowed.

Sen, C.K., Biochemical Pharmacology, is cited to show further the state of the art.

Any inquiry concerning this communication or earlier communications from the Examiner should be directed to Phyllis G. Spivack whose telephone number is 571-272-0585. The Examiner can normally be reached from 10:30 to 7 PM.

If attempts to reach the Examiner by telephone are unsuccessful, the Examiner's supervisor, Ardin Marschel, can be reached 571-272-0718. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should

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you have questions on access to the Private PAIR system, contact the Electronic

Business Center (EBC) at 866-217-9197 (toll-free).

May 20, 2006

A handwritten signature in black ink that reads "Phyllis Spivack". The script is cursive and fluid.

Phyllis Spivack

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**PHYLLIS SPIVACK
PRIMARY EXAMINER**